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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/031,801	03/15/93	KUCHERLAPATI	R A-CELL-4.4-U

HM22/1004

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EXAMINER

BECKERLEG, A

ART UNIT	PAPER NUMBER
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1632

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DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File

Office Action Summary

Application No.
08/031,801

Applicant(s)

Kucherlapati et al.

Examiner

Anne Marie S. Beckerleg

Group Art Unit

1632



☒ Responsive to communication(s) filed on Mar 6, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 68, 83-88, 95-97, and 104-109 is/are pending in the application.

Of the above, claim(s) 68 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 83-88, 95-97, and 104-109 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

file

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DETAILED ACTION

Applicant's amendment filed pursuant to 37 CFR 1.129 (a) has been entered. The finality of the previous office action has been withdrawn. Claims 89-94 and 101-103 have been canceled. Claims 83-88 and 95-97 have been amended and new claims 104-109 have been entered. Claims 68, 83-88, 95-97, and 104-109 are pending in the instant application. Claim 68 has been withdrawn from prosecution. Claims 83-88, 95-97, and 104-109 are active in the instant application. An action on the merits follows.

Claim Rejections - 35 USC § 112

The rejection of claims 83-88 and 95-97 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained in part over claims 83-88, 95-97, and new claims 104-109.

Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection for the following reasons. The applicant argues that the newly amended claims and new claims 104-109 are now directed to germline human heavy chain sequences derived from or identical to that of human chromosome 14 wherein the sequence comprises the D segment genes, the J segment genes and the constant region genes through Cu, and further wherein the sequence does not include a gamma constant region and is operably linked to at least one human V segment gene, and as such, the examiner's concerns regarding the

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disclosure of a transgene spanning the entire human Ig locus is obviated. The applicant further argues that the specification describes a transgene with the newly claimed limitations in Figure 16 and in examples 6 and 7. While the applicant's amendments to the claims do render moot the concerns regarding the stability of YACs encoding the switch regions and constant regions 3' of the C μ gene, the claims as amended continue to read broadly on germline segments of the Ig heavy or light chain locus including the D segment and J segment genes and the C μ constant region operably linked to one or more human V segment genes which can include the entire Ig locus minus the switch regions and constant regions 3' of the C μ gene. The specification, including the working examples and Figure 16, discloses a single YAC vector which comprises a Spe restriction fragment of the germline human heavy chain Ig locus which includes V6, the D segment genes, the J segment genes, C μ and C δ . The specification does not provide sufficient guidance concerning the construction of YAC vectors including additional V segments up to and including the entire V region. At the time of filing, physical mapping, cloning, and sequencing of the entire human heavy chain variable locus had not been accomplished. Further, unlike the D and J segment genes, the V segment genes are not limited to chromosome 14, but are also found on chromosomes 15 and 16. In addition, as late as 1993, the actual number of functional V segment genes was unknown and complicated by the presence of large numbers of non-functional pseudogenes (Matsuda et al. (1993) Nature Genetics, Vol. 3, 88-94). The specification provides no guidance as to V segment genes present on chromosomes 15 and 16 or provides guidance as to the sequence of variable regions distal to the D heavy chain region on chromosome 14. The

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specification does not provide guidance for obtaining YACs which include the germline sequence of chromosome 14 that comprises variable regions genes other than the YAC disclosed in Figure 16, or provide guidance for functional heavy chain variable gene sequences which could be linked to the germline sequence shown in Figure 16. Thus, the specification only teaches a single YAC vector useful for the instant invention and fails to teach how to make a YAC or any other vector which comprises the germline sequence of chromosome 14 including the entire D region and J region genes, the C μ region, and any or all variable region genes. Therefore, in view of the lack of teachings in both the art and the specification for the complete sequence of the functional V segment genes on chromosomes 14, 15, and 16, the lack of guidance for operably linking nucleotide sequences encoding V genes distal to the D heavy region or V genes present on chromosomes 15 and 16, the lack of guidance for any YAC vector other than that disclosed in Figure 16, and the breadth of the claims, the skilled artisan would not have predicted success in obtaining a YAC or any other DNA sequence encoding the germline D region, J region, and C μ gene operably linked to any or all V segment genes and as such it would have required undue experimentation to practice the invention as claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 86-88, 95-97, and 104-109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed DNA sequences that contain a germline DNA sequence of human chromosome 14 comprising the D segment genes, the J segment genes, and C μ operably linked to at least one V segment gene. The specification lacks written description for functional V segment genes distal to the D segment genes on chromosome 14 and for V segment genes present on chromosomes 15 and 16. In particular, the specification lacks written description for germline V segment gene sequences from these chromosomal regions. At the time of filing, the actual number and sequences of the functional human heavy chain V region genes had not been determined.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is claimed.” (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). In the absence of any description of genes or nucleic acids encoding V region genes from chromosomes 15 and 16 or of germline portions distal to the D region on chromosome 14 which encodes functional V segments, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides which are required to make the mice of the instant

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invention, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. Therefore, the specification does not meet the written description provision of 35 U.S.C. 112, first paragraph, for DNA sequences encoding any or all V segment genes. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

Claim Rejections - 35 USC § 102

The rejection of claims 83 and 85 under 35 USC 102(e) over U.S. Patent No. 5,591,669, hereafter referred to as Krimpenfort et al. is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for the following reason. The applicant's argue that since the claims have been amended to include language which has been found acceptable in U.S. Patent No. 5,939,598, that these present claims should also be considered patentable for the same reasons the claims in the 5,939,598 patent were found patentable. The applicant is reminded that the prosecution of each case is independent and that arguments found persuasive in a related application cannot be considered if they have not been submitted and made of record in the instant application.

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Claim Rejections - 35 USC § 103

The rejection of claims 84, 86-88, and 95-97 under 35 U.S.C. 103 over U.S. Patent No. 5,591,669 as applied to claims 83 and 85 above and further in view of U.S. Patent No. 5,591,669, hereafter Krimpenfort et al., is maintained over claim 84. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection. The applicant's arguments are the same as those expressed above in the rejection of claims 83 and 85 over Krimpenfort et al. As stated above, specific arguments concerning the applicability of Krimpenfort et al. need to be made of record in the instant application in order to be considered.

The rejection of claims 84, 86-88, and 95-97 under 35 U.S.C. 103 over U.S. Patent No. 5,591,669 in view of Bruggemann et al. and U.S. Patent No. 5,545,806 is withdrawn in view of applicant's amendments to the claims and in view of applicant's arguments concerning Bruggemann et al.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-

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9156. The examiner can be reached Mon-Thurs and every other Friday from 8:30-6:00. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196.

The official fax number is (703) 308-4242.

Dr. A.M.S. Beckerleg

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